

[received by the International Bureau on 14 March 2005 (14.03.05);
claims 1 and 82 replaced by new claims 1-44 (7 Pages)]

1. Use of a ghrelin-like compound or a pharmaceutically acceptable salt thereof for the preparation of a medicament for the prophylaxis or treatment of cancer cachexia in an individual in need of such treatment,
5 wherein the ghrelin-like compound comprises a structure defined by formula I



10 Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

15 X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

20 each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

25 Z^2 is an optionally present protecting group,

m is an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35,

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and wherein:

- (a) said ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in length, with the proviso that said ghrelin-like compound is at least 80 % homologous to SEQ ID NO 1, such as at least 85
35 % homologous to SEQ ID NO: 1

and/or

(b) said ghrelin-like compound is at least 90 % homologous to SEQ ID NO 1.

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2. The use according to claim 1, wherein said ghrelin-like compound is at least 95 % homologous to SEQ ID NO 1.

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3. The use according to claim 1, wherein said ghrelin-like compound is at least 98 % homologous to SEQ ID NO 1.

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4. The use according to any of the preceding claims, wherein m is an integer in the range of from 1-9, such as of from 1-8, such as of from 1-7, such as of from 1-6, such as of from 1-5, such as of from 1-4, such as of from 1-3, such as of from 1-2, such as 2.

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5. The use according to any of the preceding claims, wherein X^2 is selected from the group of modified Ser, modified Cys and modified Lys, such as wherein X^2 is modified Ser.

6. The use according to any of the preceding claims, wherein the ghrelin-like compound is selected from a compound of

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formula II $Z^1 - \text{Gly} - (X^1)_{m-1} - (X^2) - (X^3)_n - Z^2$,

formula III $Z^1 - \text{Gly} - \text{Ser} - (X^2) - (X^3)_n - Z^2$, and

formula IV $Z^1 - \text{Gly} - (X^2) - (X^3)_n - Z^2$.

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7. The use according to claim 6, wherein the ghrelin-like compound is having formula III.

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8. The use according to any of the preceding claims, wherein n is an integer in the range of from 1-25, such as of from 1-24, such as from 1-15, such as of from 1-10, such as of from 10-25, such as of from 10-24, such as of from 15-25, such as of from 15-24.

- 5 9. The use according to any of the preceding claims, wherein the acyl group is selected from a C1-C35 acyl group, such as a C1 – C20 acyl group, such as a C1 – C15 acyl group, such as a C6 – C15 acyl group, such as a C6 – C12 acyl group, such as a C8 – C12 acyl group.
- 10 10. The use according to any of the preceding claims, wherein the acyl group is selected from the group of C7 acyl group, C8 acyl group, C9 acyl group, C10 acyl group, C11 acyl group, and C12 acyl group.
- 11 11. The use according to any of the preceding claims, wherein the acyl group is selected from the group of C8 acyl group, and C10 acyl group.
- 15 12. The use according to any of the preceding claims, wherein the acyl group is selected from the group of C7 acyl group, C9 acyl group, and C11 acyl group, such as from the group of C9 acyl group and C11 acyl group.
- 20 13. The use according to claim 1, wherein the ghrelin-like compound is ghrelin or a pharmaceutically acceptable salt thereof.
- 25 14. The use according to claim 1, wherein the ghrelin-like compound has SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3.
- 30 15. The use according to any of the preceding claims, wherein the medicament is in a formulation for subcutaneous administration.
- 35 16. The use according to any of the preceding claims, wherein the formulation comprises the ghrelin-like compound or a salt thereof as a lyophilisate and the formulation further comprises a solvent, said lyophilisate and said solvent being in separate compartments until administration.
17. The use according to any of the preceding claims, wherein the formulation is a solution of the ghrelin-like compound or a salt thereof.
18. The use according to claim 16 or 17, wherein the solvent is saline.

19. The use according to any of the preceding claims, wherein the medicament is administered prior to or during a meal.

5 20. The use according to any of the preceding claims, wherein the medicament is administered in a concentration equivalent to from 10 ng to 10 mg ghrelin per kg bodyweight.

10 21. The use according to claim 20, wherein the medicament is administered in a concentration equivalent to from 0.1 µg to 1 mg ghrelin per kg bodyweight, such as from 0.5 µg to 0.5 mg ghrelin per kg bodyweight, such as from 1.0 µg to 0.1 mg ghrelin per kg bodyweight, such as from 1.0 µg to 50 µg ghrelin per kg bodyweight, such as from 1.0 µg to 10 µg ghrelin per kg bodyweight.

15 22. The use according to claim 21, wherein the medicament is administered in a concentration equivalent to from 0.1 µg to 1 mg ghrelin per kg bodyweight, such as from 0.5 µg to 0.5 mg ghrelin per kg bodyweight, such as from 1.0 µg to 0.1 mg ghrelin per kg bodyweight, such as from 1.0 µg to 50 µg ghrelin per kg bodyweight, such as from 1.0 µg to 10 µg ghrelin per kg bodyweight.

20 23. The use according to any of the preceding claims, wherein the medicament is administered as a bolus prior to or during a meal, said bolus comprising an amount of the ghrelin-like compound or a salt thereof equivalent to from 0.3 µg to 600 mg ghrelin

25 24. The use according to claim 23, wherein the medicament is administered as a bolus prior to or during a meal, said bolus comprising an amount of the ghrelin-like compound or a salt thereof equivalent to from 2.0 µg to 200 mg ghrelin, such as from 5.0 µg to 100 mg ghrelin, such as from 10 µg to 50 mg ghrelin, such as from 10 µg to 5 mg ghrelin, such as from 10 µg to 1.0 mg ghrelin.

30 25. The use according to any of the preceding claims, wherein the medicament is administered from one to three times daily, each administration being during a meal or at the most 180 minutes prior to a meal, such as at the most 90 minutes prior to a

meal, e.g. at the most 45 minutes prior to a meal, such as at the most 30 minutes prior to a meal, such as at the most 25 minutes prior to a meal, such as at the most 20 minutes prior to a meal, such as at the most 15 minutes prior to a meal, such as at the most 10 minutes prior to a meal, such as at the most 5 minutes prior to a meal.

26. The use according to claim 25, wherein the medicament is administered three times daily.

27. The use according to any of the preceding claims, wherein the cancer cachexia is caused by a catabolic disorder.

28. The use according to any of claims 1 to 26, wherein the cancer cachexia is caused by an anorectic disorder.

29. The use according to any of claims 1 to 27, where the individual is suffering from a cancer selected from lung cancer, pancreatic cancer, liver cancer, and GI tract cancers.

30. Use according to any of the preceding claims, wherein said medicament is administered in combination with a chemotherapy medicament.

31. The use according to any of the preceding claims, wherein the treatment or prevention of cancer cachexia leads to stimulation of appetite, stimulation of food intake, stimulation of weight gain or weight maintenance, and/or increased body fat mass.

32. A method for preventing or treating cancer cachexia, comprising administering to an individual in need thereof an effective amount of a ghrelin-like compound as defined in any of claims 1-14.

33. A method for preventing or treating cancer, comprising administering to an individual in need thereof an effective amount of a secretagogue as defined in any of claims 1-14, in combination with an anti-neoplastic treatment.

34. The method according to claim 33, wherein the antineoplastic treatment is radiotherapy.

35. The method according to claim 33, wherein the antineoplastic treatment is chemotherapy.

36. The method according to any of claims 33-35, wherein the treatment or prevention of cancer cachexia leads to stimulation of appetite, stimulation of food intake, stimulation of weight gain or weight maintenance, and/or increased body fat mass.

37. A method for preventing or treating cachexia, comprising administering to an individual in need thereof an effective amount of a ghrelin-like compound and an effective amount of a NSAID medicament.

38. The method according to claim 37, wherein the ghrelin-like compound is as defined in any of claims 1 to 14.

39. Use of a ghrelin-like compound or a pharmaceutically acceptable salt thereof for the preparation of a medicament, in a formulation for subcutaneous administration, for stimulation of appetite in an individual by administering a subcutaneous dosage of said medicament to the individual,

wherein the ghrelin-like compound comprises a structure defined by formula I

$Z^1 - (X^1)_m - (X^2) - (X^3)_n - Z^2$, wherein

Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

5 wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

Z^2 is an optionally present protecting group,

10 m is an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35.

40. Use according to claim 39, wherein the ghrelin-like compound is as defined in any of claims 1-14.

15 41. Use according to claim 40, wherein the formulation is as defined in any of claims 15-19.

42. Use according to claim 41, wherein the solvent is saline.

20 43. Use according to any of claims 39 to 42, wherein the medicament is administered as defined in any of claims 19-26.

44. Use according to any of claims 39-43, wherein said individual is suffering from lipodystrophy.